

REMARKS**I. STATUS OF THE CLAIMS**

Claims 1, 3-40, 44-62 and 66-91 are pending, claims 2, 41-43 and 63-65 having been previously canceled, and claims 5, 6, 19-40, 44-62 and 66-91 having been withdrawn from consideration as drawn to non-elected embodiments. With this Amendment, claims 1, 14, 15, 34 and 44 are amended. Claims 3, 4, 6, 7, 11, 30, 50, 57 and 87 are canceled herewith, without prejudice against their reintroduction into this or one or more timely filed continuation, divisional or continuation-in-part applications. Thus, after entry of this Amendment, claims 1, 5, 8-10, 12-29, 31-40, 44-49, 51-56, 58-62, 66-86 and 88-91 remain pending, with claims 1, 5, 8-10 and 12-18 currently under consideration, with claims 19-29, 31-40, 44-49, 51-56, 58-62, 66-86 and 88-91 remaining withdrawn. The amendments of the claims and the various rejections raised in the Office Action are discussed in more detail, below.

II. AMENDMENTS

Claims 1 and 44 are amended to incorporate the limitations of claims 3 and 4, which are canceled accordingly.

Claim 45 is amended to correct a dependency.

Claims 14, 15, 34 and 61 are amended to remove reference to "gene 6."

Claims 6, 7, 11, 30, 50, 57 and 87 are canceled.

No new matter is added by way of the amendments presented herein.

III. CLAIM REJECTIONS UNDER 35 USC §102

Claims 1, 3, 4, 8-12, 17 and 18 remain rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Horsburgh *et al.* (US Patent 6,277,621 B1, "Horsburgh").

Applicants respectfully note that there are clear structural and functional differences between Herpes Simplex Virus (HSV) described in Horsburgh. and VZV of the present claims. The HSV-1, HSV-2, VZV, CMV, EBV, HHV6, or HHV7 viruses described in Horsburgh column 3, lines 47-49 and asserted by the Examiner as anticipatory relate to wild type strains, rather than to "live attenuated recombinant varicella-zoster virus" or "vaccine." The disclosure of Horsburgh is not applicable to or predictive of the present subject matter in which a live attenuated recombinant VZV using non-essential gene regions is produced. Horsburgh discloses artificial chromosome constructs containing HSV sequences. The present claims are

directed to VZV. Applicants respectfully note that these viruses are not directly comparable such that one can assume, as the Examiner does, that a HSV gene and a VZV gene such as UL13 (see Office Action at page 3) are homologous.

Herewith, Applicants are submitting a Declaration under 37 C.F.R. § 1.132 by one of the named inventors of the present application, Dr. Kazuhiro NAGAIKE, attesting to representative experiments which were used to determine the specific gene regions of the VZV genome non-essential for expression, wherein it was confirmed that a disruption of gene 13, for example, by inserting a kanamycin resistance gene still allowed the virus to proliferate and produce infective viral particles; thus, gene 13 was identified as non-essential. Table II in the declaration also illustrates this fact, by comparing non-essential gene regions such as those disclosed in Horsburgh to those of the instant invention. Note that VZV gene 13 has no counterpart in HSV, and UL13 cited by the Examiner is VZV 47, a protein kinase Tegument protein.

Further, as amended, the claims relate to the insertion of BAC sequences into "a region flanking" non-essential genes, and recite the specific non-essential gene region(s) relating to the Oka strain. In contrast, Horsburgh describes recombination "in the ORF region" of a gene. Horsburgh does not envisage Applicants' advantageous effect of preventing disruption of the gene into which the BAC vector is inserted (*i.e.* gene 13 following insertion maintains its function).

Finally, to refute the Examiner's assertion on pages 4-5 of the Final Office Action that "(a)lthough Horsburgh does not specifically suggest that the viruses be used as pharmaceutical compositions or vaccines,...Applicant has not presented any evidence or reasoning why Horsburgh's suggestion to use the BAC constructs to produce live, attenuated viruses is not enabled," Applicants respectfully direct the Examiner's attention to point 6 of the Declaration by Dr. NAGAIKE. Here, Dr. NAGAIKE notes that the HSV vector of Horsburgh would be ineffective as a vaccine, because the safe use of HSV requires acyclovir to guard against uncontrolled viral proliferation, and the TK gene is disrupted in the HSV vector produced according to Horsburgh. In contrast, the VZV Oka vaccine strain of the present invention is an attenuated live vaccine developed as a medicament, where safety in its utility is guaranteed without the use of acyclovir.

In all these ways, Applicants' claims clearly define over Horsburgh. Applicants respectfully request reconsideration and withdrawal of the novelty rejection.

IV. CLAIM REJECTIONS UNDER 35 USC §103

Claims 13, 14 and 15 remain rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Horsburgh, as applied to claim 1 above, and further in view of the abstract of PCT Publication WO00/50603 (hereinafter, "WIPO abstract").

Claims 7 and 16 remain rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Horsburgh, as applied to claim 1 above, and further in view of Mori *et al.* (US Patent Application Publication 20080226677, filed May 12, 2004, hereinafter, "Mori").

The obviousness rejections rely on Horsburgh as a primary reference, and the WIPO abstract and Mori fail to cure the deficiencies of Horsburgh. None of the cited documents, alone or in combination, teach the specified gene region(s) of an Oka strain for insertion of BAC vector sequences and production of an attenuated recombinant live varicella virus and vaccine thereof with the demonstrated advantageous effects.

Applicants respectfully request reconsideration and withdrawal of the obviousness rejections.

V. DOUBLE PATENTING

Claims 1, 3, 4 and 7-18 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly being unpatentable over claims 1, 4, 11-17, 24 and 25 of co-pending Application No. 12/094,757.

Applicants again respectfully request that this provisional obviousness-type double-patenting rejection be held in abeyance until patentable subject matter is found in one of the co-pending applications, or until the other rejections in the present case are overcome and the claims of this case are otherwise in condition for allowance.

As noted by the Examiner, the rejection was provisional precisely because the claims of the cited applications have not, in fact, been patented. It is improper for the Examiner to maintain a provisional obviousness-type double-patenting rejection based on claims that have not been allowed or issued in a patent. Until patentable subject matter is found in the applications not yet granted and serving as the basis of the provisional rejection under the judicially created doctrine of obviousness-type double patenting, the claims of the instant application should be considered on their merits. Furthermore, as stated in the Manual for Patent Examining Procedure, "(i)f the 'provisional' double patenting rejection in one application is the only rejection remaining in that application, the examiner should then withdraw the rejection and permit the application to issue as a patent" (M.P.E.P. 804(I)(B)).

Thus, Applicants again respectfully request withdrawal of this provisional obviousness-type double-patenting rejection, and request that the claims of the instant application be considered on their merits.

Applicants reserve the right to file a terminal disclaimer in the event that it is deemed necessary in a later stage of prosecution.

VIII. CONCLUSION

In view of the foregoing, Applicants submit that the claims pending in the application are in condition for Allowance. A Notice of Allowance is therefore respectfully requested.

No fees are believed to be due in connection with this Amendment. However, the Commissioner is authorized to charge any additional fees that may be required, or credit any overpayment, to King & Spalding LLP Deposit Account No. 50-4616.

If a telephone conference would expedite the prosecution of the subject application, the Examiner is requested to call the undersigned at (650) 590-1932.

Respectfully submitted,
KING & SPALDING LLP

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